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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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|-----------------|-------------|----------------------|---------------------|

09/348,354 07/07/99 HAVENGA

M 4123US

HM12/1029

EXAMINER

BRUNOVSKIS, P

| ART UNIT | PAPER NUMBER |
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1632

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DATE MAILED: 10/29/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

| | | |
|-----------------------------|------------------------|---------------------|
| Offic Action Summary | Application No. | Applicant(s) |
| | 09/348,354 | HAVENGA ET AL. |
| | Examiner | Art Unit |
| | Peter Brunovskis | 1632 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 17 October 2001.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-3,9-11 and 13-32 is/are pending in the application.
- 4a) Of the above claim(s) 13-32 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-3 and 9-11 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>16</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The request filed on 10/17/01 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/348,354 is acceptable and a CPA has been established. An action on the CPA follows.

Amendment of claim 2 (as previously filed in the after final amendment of 8/16/01) is acknowledged. Claims 13-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention by original presentation in accordance with Paper No. 14, filed 4/17/01.

Any objections or rejections made in a previous Office Action that are not herein reinstated have been withdrawn. Unless otherwise indicated, arguments directed to rejections rendered moot by Applicants amendments or Examiner's withdrawal will not be further addressed or acknowledged. Claims 1-3 and 9-11 are under examination in the instant application.

Information Disclosure Statement

Applicants IDS documents filed 1/26/01 has been found and considered. A signed copy of the "Second Supplemental Information Disclosure Statement" filed 8/16/01, a duplicate of the 1/26/01 filing is submitted herewith. The information disclosure statement filed 8/16/01 (and 1/26/01) fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise

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explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of EP 0259212 which is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered. In addition, JP02078631, WO 93/06223, WO 93/07282, WO 93/07283, WO 94/24299, WO 96/17073, WO 96/18740, WO 96/00790, WO 96/07739, WO 96/10087 were only considered with respect to their English abstracts, since no translations were supplied.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-3 and 9-11 remain rejected under 35 U.S.C. 102(e) for the reasons set forth in the Office Action of 10/24/00 and for the reasons set forth below as being anticipated by Crystal et al. (US 6,127,525).

Applicant's arguments filed 10/17/01 (repeating the arguments of 8/16/01) have been fully considered but they are not persuasive. The response argues "that it is inappropriate to cite the inherency in Crystal of a 'particular tropism adapted for a particular plurality of target cells in

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a host' when Applicants have claimed fiber protein having desired tropism" (paragraph abridging p. 7-8). The response further asserts that "[i]n order for Crystal to anticipate this element of the claimed invention, it must either expressly or inherently describe fiber protein having desired tropism, not just a particular tropism. While it is true that in the entire universe of adenoviral fiber proteins, each different fiber protein will exhibit a particular tropism, it is not the case that all fiber proteins will exhibit a tropism that is desirable for a given application...[and that]...[t]his distinction is important to applicants' claimed invention and is not described in Crystal" (top of p. 8).

To the contrary, Crystal points out that recombinant adenoviral vectors (as in the disclosed invention) "are additionally preferred based on their normal tropism for the respiratory epithelium in cases where the targeted tissue for somatic gene therapy is the lung" (col. 1, lines 37-40). Since the adenoviral vectors disclosed contain a fiber "adapted" for such a tropism and since Crystal discloses variants in the fiber, coat, and/or penton base proteins responsible for tissue tropisms and/or immunogenicities, the disclosure of Crystal clearly anticipates the claimed subject matter of the instant invention. Inasmuch as Crystal implicitly teaches that adenoviral vectors of the disclosed invention have a desirable tropism for respiratory epithelium, Crystal meets the intended use limitation in the recited claims of the instant application.

The response concedes that "[i]n order for Crystal to anticipate this element of the claimed invention [i.e. desired tropism], it must either expressly *or inherently* described fiber protein having desired tropism, not just a particular tropism" (top of p. 8; emphasis added). As

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pointed out in the Office Action of 4/17/01 in accordance with MPEP 2112, “[o]nce a reference teaching product appearing to be substantially identical is made the basis of a rejection and the examiner presents evidence or reasoning tending to show inherency, the burden shifts to the applicant to show an obvious difference”. However, the response fails in its burden to point out any *structural difference* between the claimed invention and the prior art, so as patentably distinguish the claimed invention from the prior art. The mere recitation of an intended use limitation does not provide for a structural difference between the claimed invention and the prior art, particularly in view of *Ex parte Obiaya*, which teaches that even if the prior art disclosure did not recite or recognize a property or advantage that would flow naturally from following the suggestion of the prior art, this observation cannot serve as the as the basis for patentability over the prior art when the structural differences are otherwise identical. The response failed to address this argument previously set forth in the Office Action of 4/17/01.

In agreement with Applicants position on p. 8, “[o]nce the Office has established a *prima facie* case for inherency, the burden shifts to the applicant to rebut inherency with evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product”. Importantly, the response fails to rebut the *prima facie* evidence for inherency as directed to Crystal’s disclosure of an adenoviral vector comprising a fiber protein comprising a fiber protein from one adenovirus serotype, Ad5, and at least a part of a hexon protein from a second serotype, Ad7, wherein the second adenovirus serotype (i.e. Ad7) has lower relative tropism to a plurality of cells than the chimeric adenovirus (as specified by the Ad5 fiber protein)

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and wherein the second adenovirus serotype (Ad7) has less antigenicity than the first adenovirus serotype (i.e. Ad5) as evidenced by Applicants 1.132 declaration (see e.g. Figure 1) *and Table 2, p. 73 of the instant specification*, which clearly illustrates a difference in tropism between the two, depending on the type of tropism deemed “desirable”. The *specifications’* teachings constitute adenoviral tissue tropism is germane to the question of inherency, not whether Crystal mentions such tropisms or whether Dr. Havenga’s declaration makes any reference to tissue tropism as argued in the response (top of p. 9).

It is important to note that the rejected claims are not drawn to any particular “desired tropism”; rather, the recited claim limitation is merely a statement of intended use wherein the measure of “desirability” is highly subjective. What can be deemed desirable for one application would be undesirable for another. Given that modified fibers exhibit diverse patterns of tropism, it is not hard to envision multiple embodiments within the broad scope of Applicants claimed invention that would be anticipated by the disclosure of Crystal, particularly in view of Applicants own evidence concerning inherent tropisms and antigenicities of the various adenoviral serotypes.

Inherency, in the instant case is not based on probabilities or possibilities, but rather Applicants own evidence which substantiates Crystal’s disclosure as anticipating the subject matter as claimed. Moreover, the fact that Applicants may have recognized certain characteristics concerning specific adenoviral tropisms or antigenicities does not obviate the grounds for rejection under inherency, particularly when the invention is so broadly claimed as in

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the instant case. Determining whether a prior art disclosure anticipates the claimed *compositions* depends on evaluating whether a given composition meets the structural and functional limitations recited therein, independent of whether the disclosure itself reveals the distinction. The Office has met its burden in establishing a prima facie case for anticipation based on both a broad interpretation of the claims and evidence concerning inherency as set forth in the Office Action of 4/17/01 and as set forth herein.

No claims are allowed.

All claims are drawn to the same invention claimed in the parent application prior to the filing of this Continued Prosecution Application under 37 CFR 1.53(d) and could have been finally rejected on the grounds and art of record in the next Office action. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing under 37 CFR 1.53(d). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will

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the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX number is (703) 308-4242 or 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Brunovskis whose telephone number is (703) 305-2471. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda can be reached at (703) 305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to the Patent Analyst, Patsy Zimmerman whose telephone number is (703) 308-8338.

Peter Brunovskis, Ph.D.
Patent Examiner
Art Unit 1632

Deborah Crouch
DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1800-1630